



Case Report

Identification at autopsy of pulverized pills in lungs of a first-time methadone user

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ABSTRACT

We recently encountered a 25-year-old white man who died of substance abuse including methadone. The route of administration of the drug(s) appears to have been insufflation. He was found dead at home. There were bottles of prescribed medications and an empty bottle of non-prescribed methadone. There was a grinding device nearby. At autopsy, no needle tracts were identified. Microscopically, the bronchi had desquamated ciliated respiratory epithelium admixed with red-brown pigment, which was found under plane-polarized light to be comprised of birefringent finely-granular material consistent with pulverized pills. Blood toxicology was positive for tetrahydrocannabinol, sertraline, nicotine, and methadone. The cause of death was ruled drug interactions with cerebral and pulmonary edema, the manner of death accidental. The decedent fit a profile of a victim of prescription drug abuse, for whom the mode of administration of drugs may be altered from intended use in as many as 80% of cases.

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1. Introduction

Methadone is a synthetic opioid used for maintenance of withdrawal and management of narcotic addicts, as an antitussive, and as a treatment for non-cancer pain.¹ In the USA, methadone is usually administered orally.

We recently encountered a 25-year-old man who died of substance abuse including a medication for which he had a legal prescription and methadone, for which he had no prescription and no known history of abuse. While intoxication and death from multiple substances is not unusual in forensic practice,² the route of administration of the drug(s) in this case appears unusual. No identifiable pill contents or fragments were found in the decedent's gastrointestinal tract, but the bronchi and bronchioles were diffusely strewn with finely-granular foreign material that was birefringent under plane-polarized light, consistent with pills that had been ground into a powder and insufflated.

We report this case as an unusual example of fatal drug interaction by a rare mode of administration.^{3,4} More strikingly, the case demonstrates anatomic evidence of the presence of the foreign substance(s) in the bronchi, a finding that has rarely been previously demonstrated.⁵ We further examine the patterns of methadone use and abuse in the literature.

2. Case report

The decedent was a 25-year-old white man who lived at home with his mother. She reported that he was treated medically for anxiety disorder with oral sertraline. He was known to smoke marijuana, but had no other known substance abuse issues. He had not previously used drugs or any other method to harm himself. His only previous complication of drug use had been an overdose of a cold medication he had experienced several years previously. The decedent was reported to have an intense interest in pills of all kinds, and believed he was quite knowledgeable about pills and medications.

The decedent had seen his physician for a cold the previous day, for which he was given a prescription for antibiotics that he had not filled. His mother last saw him alive the evening antemortem around 10 pm. When she left the next morning, she noted his door was closed, and she assumed he was sleeping. She returned in the afternoon to find his door was still closed. She entered the room to try to rouse him, but found him in bed, clothed, cold and unresponsive. Emergency personnel were summoned, but they were unable to resuscitate him. He was declared dead at the scene.

On his nightstand were several bottles of medications prescribed to him that were partially consumed, including lorazepam, buspirone, and sertraline. The third bottle was nearly empty. He also had over-the-counter preparations of guaifenesin and melatonin. There was also an empty bottle of methadone that was identified by a client number. He had no prescription for methadone and was not known to have used it previously.

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Inspection of the room demonstrated a closet with containers full of empty pill bottles (Fig. 1), a “one-hitter” pipe with marijuana residue in it, and a grinding device designed to shred marijuana in a box near his bed (Fig. 2). There were no straws or empty pens that are commonly used for powder insufflation, but there was the pipe that was hollow and there were many pieces of paper that could have been rolled for that purpose.

The body was transferred to a hospital morgue for autopsy. On external examination, no needle tracts were identified. There was no vomitus on the decedent or reportedly on his bed or in his room. The nares were impacted with thick mucus. The significant internal gross findings were marked cerebral and pulmonary edema (Fig. 3), a calcified granuloma of the right lung, and concentric hypertrophy of the heart. No pills were identified in the stomach contents or upper gastrointestinal tract. Microscopically, the lungs were notable for desquamation of the ciliated respiratory epithelium admixed with red-brown pigment suggestive of hemosiderin (Fig. 4). Under plane-polarized light, however, the pigment was found to be comprised of birefringent finely-granular foreign material that was consistent with pulverized pills (Fig. 5). Blood toxicology studies were positive for tetrahydrocannabinol and metabolite, 1.3 ng/mL; sertraline, 472 ng/mL (therapeutic range 30–200 ng/mL); nortriptyline, 2817 ng/mL (no therapeutic range established); nicotine and cotinine; and methadone, 450 ng/mL (therapeutic range 50–1000 ng/mL). Tissue assay of the lung for methadone was negative.

It was concluded that drug interactions and subsequent cerebral and pulmonary edema were the cause of death. The manner of death was determined to be accident.

3. Discussion

Drug interactions and polysubstance abuse are often found in cases of unexpected death in decedents where no anatomic cause of death is evident.² Routes of administration of the substances may be oral, smoking, intravenous, or insufflation.^{3,4} The drugs used may be illicit or prescription drugs, and the mode of administration may be altered from intended use in as many as 80% of cases.^{3,4}

The present decedent fits a profile of a victim of prescription drug abuse. They are commonly young rural Caucasian men, smokers, and suffer from psychiatric problems such as anxiety, depression, or post-traumatic stress disorder.³ Up to half are also drinkers, and many have a history of polysubstance abuse.³ This decedent was slightly younger than the mean age of prescription



Fig. 1. Scene investigation. Closet with jars filled with empty pill bottles. Additional bottles with medications present were located at bedside, including one that was identified in postmortem toxicology (sertraline).



Fig. 2. Scene investigation. Grinder found in box near bed. Since pill insufflation was not suspected, the only substance grossly sought was residual shredded marijuana, which was confirmed. Empty plastic bags in the box were probably previous marijuana purchases.



Fig. 3. Gross examination of organs. Left lung, cut surface. Note foamy edema of with distended bronchioles peripherally.

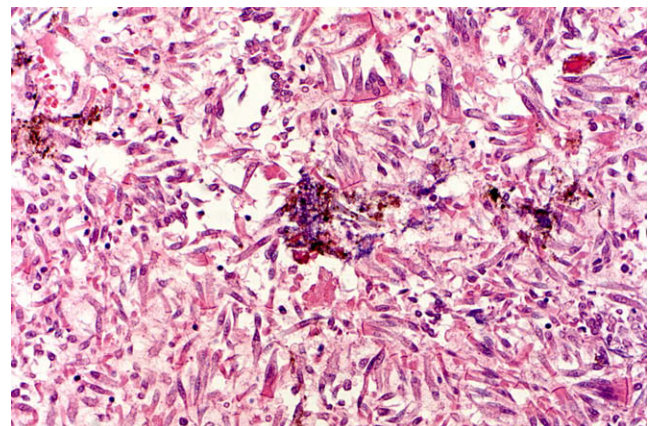


Fig. 4. Microscopic examination of lung, brightfield. Desquamated bronchial epithelium fills field, a normal postmortem finding. The cilia, terminal bars, and pseudostratified columnar epithelium are maintained. Red-brown pigment, noted peripherally and centrally in the field, was presumed to be hemolyzed red cells (hematoxylin and eosin, 400 \times). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

drug abusers in other studies, 29.3 years,⁴ and 30.95 years,³ but fit most of the other observations in the profile.

In large studies, 60% of abusers of prescription drugs typically began their drug use because of chronic pain.³ Most abusers,

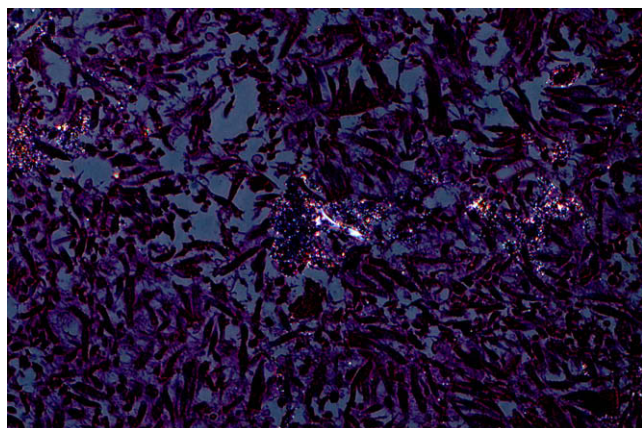


Fig. 5. Microscopic examination of lung, polarized light. The presumed hemosiderin pigment consists of multiple, widely disseminated particles of polarizable foreign material consistent with fragments of crushed pills. Different sizes and shapes of the particles suggest uneven pulverization. Some relatively long fiber-like fragments may represent residual marijuana fibers from the grinder (hematoxylin and eosin, 400 \times).

92.84%, were introduced to narcotics with a legitimate prescription for hydrocodone and oxycodone, and occasionally for methadone or fentanyl.³ Among users of illicit drugs, heroin or non-prescribed methadone are common drugs of abuse.⁴ After dependency or addiction are established, a large majority of abusers, 99.91%, purchase additional drugs illegally on street; others borrow them from other users, or steal them.³ The present decedent did not have a problem of chronic pain, but of anxiety. It is not clear if he deliberately took an increased dose of sertraline, although the blood concentrations of this drug exceeded therapeutic limits, the norsertraline concentration was very high, and he had fewer pills than expected in his bottle. The lack of pills in the stomach or gastrointestinal tract contents suggests these pills, which he was known to take orally, were taken earlier, and had reached high serum concentrations by the time of death. He had no previous known experience with narcotics. However, he clearly obtained methadone illicitly, either for experimentation or in the belief that it would augment his other treatment.

As noted, once a drug abuser obtains substances illicitly, there is a high likelihood that he or she will alter the intended route of administration.^{3,4} This trend may be due to the experimentation that accompanies the acquisition of new or more drugs. Among drugs that are obtained, cocaine and amphetamines are usually injected or snorted,⁴ while methadone and benzodiazepines tend to be taken orally, rarely injected.⁴ Methadone insufflation has been observed clinically and forensically, however. A study of known methadone and toluene insufflation studied by scanning electron microscopy showed 0.15–0.20 μ M particles that were consistent with paint material, implying previous non-fatal insufflation.⁵

Such sophisticated technologies were not available to us, so we relied on light microscopy and previous work with methadone and related substances to analyze our findings. We were not surprised, for example, that the lung parenchyma was negative for methadone on tissue assay, so that only pill matrix was left in the lungs. Insufflated narcotics appear to be absorbed rapidly, and the decedent most likely survived a certain period of time before the drug–drug interactions became lethal. For example, a related synthetic opioid, fentanyl, can be administered by inhalation in liposome-encapsulated fentanyl or aerosolized forms, and the effects of drug concentration can be monitored clinically. Both methods lead to rapid serum increases in serum narcotics.^{6,7} By contrast, organ concentration of drugs of abuse is variable, notably in the left posterior liver and in limited amounts in the left posterior basal

lung.⁸ Thus, we expect rapid absorption of narcotics via pulmonary route with little residual drug in the parenchyma, and unreliable measures of residual drug in the tissue except in very limited areas. If the decedent survived some period after the insufflation, which we can surmise from the arrival of neutrophils in the bronchi, we could expect the drug to have been absorbed, and the non-absorbable pill matrix to remain.

This decedent did not survive his drug use. Thus, the presence of insufflated powder from ground pills was found in his lungs, and blood toxicology confirmed the presence of medications that were in his possession, methadone, sertraline plus metabolite, and marijuana and metabolite. He was accustomed to taking the prescription drugs orally, but may have concluded that insufflation would provide more euphoria for a narcotic. The presence of a grinder near his bed suggests that this device could have been used to pulverize the medication, and insufflation was the route of administration. The presence of polarizable granular foreign material of different shapes and sizes in the bronchi is consistent with the insufflation of ground pills. There is no explanation for the administration of the drug by this route other than the observation that atypical intake of a drug appears to be part of a pattern of experimentation among substance abusers who branch into new substances.^{3,4}

In any case, this decedent demonstrates the presence of crushed material in the bronchi that were insufflated for drug intake. The lack of birefringent material in the lymphatics or blood vessels suggests that insufflation was not his practice, but was a new method that he attempted that night. The abundant production of mucus that was grossly present in his nose and tracheobronchial tree imply that the innate immune responses were attempting to clear the foreign material from his pulmonary system. Unfortunately, the types of drugs involved were sufficient to cause unintended drug interaction and death.

Conflict of Interest

There are no conflicts of interest in presenting this case.

Funding

There was no external funding for this report.

Ethical Approval

No experimentation was performed so no Institutional Review Board approval was required.

References

- Sandoval JA, Furlan AD, Mailis-Gagnon A. Oral methadone for chronic noncancer pain: a systematic literature review of reasons for administration, prescription patterns, effectiveness, and side effects. *Clin J Pain* 2005;**21**:503–12.
- Carson HJ. Classes of drugs and their prevalence in multiple drug intoxication in suicides and accidents. *Leg Med* 2008;**10**:92–5.
- Passik SD, Hays L, Eisner N, Kirsh KL. Psychiatric and pain characteristics of prescription drug abusers entering drug rehabilitation. *J Pain Palliat Care Pharmacother* 2006;**20**:5–13.
- Gossop M, Marsden J, Stewart D, Treacy S. Routes of drug administration and multiple drug misuse: regional variations among clients seeking treatment at programmes throughout England. *Addiction* 2000;**95**:1197–206.
- Byard RW, Gilbert JD, Terlet J. Death associated with volatile substance inhalation – histologic, scanning electron microscopic and energy dispersive X-ray spectral analyses of lung tissue. *Forensic Sci Int* 2007;**171**:118–21.
- Hung OF, Whynot SC, Varvel JR, Shafer SL, Mezei M. Pharmacokinetics of inhaled liposome-encapsulated fentanyl. *Anesthesiology* 1995;**83**:277–84.
- Mather LE, Woodhouse A, Ward ME, Farr SH, Rubsamen RA, Eltherington LG. Pulmonary administration of aerosolized fentanyl: pharmacokinetic analysis of systemic delivery. *Br J Clin Pharmacol* 1998;**46**:37–43.
- Pounder DJ, Adams E, Fuke C, Langford AM. Site to site variability of postmortem concentrations in liver and lung. *J Forensic Sci* 1996;**41**:927–32.